PATENT COOPERATION TREATY

PCT

REC'D 29 MAY 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P.Q. 12,768		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/00018	05/01/1999	06/01/1998
International Patent Classification (IPC) or national classification and IPC B01J19/00		
Applicant CENTRAL RESEARCH LABORATORIES LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

 ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

 - I ☒ Basis of the report
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26/07/1999	07.04.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Thomasson, P Telephone No. +49 89 2399 8339

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/00018

I. Basis of the r port

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-10 as originally filed

Claims, No.:

1-24 as received on 20/03/2000 with letter of 17/03/2000

Drawings, sheets:

1/8-8/8 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☒ the claims, Nos.: 25-27
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-22, 24
	No:	Claims	23
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-24
Industrial applicability (IA)	Yes:	Claims	1-24
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document:

 D1: WO-A-96/12541

2. Claim 23 does not meet the requirement of Article 33(2) PCT for the following reason:

 D1 is disclosing a method of connecting channels formed in a substrate (see D1: Figure 11d). Figure 11d is showing a substrate block (150) containing three horizontal channels (158) which are interconnected by vertical cuts (154).
 Therefore the subject-matter of claim 23 is not novel.

3. Claim 1 does not meet the requirement of Article 33(3) PCT for the following reasons:

3.1 D1, considered as being the closest prior art, is disclosing a multiplicity of substrate layers (see D1: Figure 11d, (152)) forming horizontal channels (158) which are interconnected by vertical cuts (154) which extend downwardly from the external surface of the top substrate layer (152).

3.2 The subject-matter of claim 1 differs from D1 in that the two substrates are bonded together prior to the cut formation. D1 is silent about this step.

3.3 The attention of the applicant is drawn to the fact that the subject-matter of claim 1 does not solve any technical problem against D1. D1 is disclosing a method of connecting channels by cut formation and provides a very compact system for processing large quantities of fluid (see D1: page 19, lines 3 and 23-24). The fact that claim 1 indicates that the cut is formed after bonding the two substrates, which is considered to be a common feature for the skilled person, especially as the advantages thus achieved (the physical integrity of the device is maintained during the cut) can readily be foreseen, cannot support any inventive step (Article 33(3) PCT).

4. The technical features of claims 2-10 are either known from D1 or are considered to be merely one of several possibilities which the skilled person would select, in accordance with the circumstances, without the exercise of inventive skill. Consequently these claims do not meet the requirement of Article 33(3) PCT.

5. As a consequence the subject-matter of claims 11 and 24 (apparatus according to the method of claims 1-10 and micro-fluidic device incorporating the apparatus) does not involve any inventive step (Article 33(3) PCT).

6. The technical features of claims 12-22 are either known from D1 or are considered to be merely one of several possibilities which the skilled person would select, in accordance with the circumstances, without the exercise of inventive skill. Consequently these claims do not meet the requirement of Article 33(3) PCT.

RECEIVED 20-03-00

Claims

1. Method of connecting channels including a) forming at least one flow path in a first substrate; b) forming at least one flow path in a second substrate; c) contacting the first and second substrates to form at least one channel; and d) forming at least one cut in an external face of the first substrate, the cut being of sufficient depth to intersect one or more of the channels such that, in use, a fluid passing along a fluid pathway defined by the at least one cut may pass into the at least one channel, characterised in that the substrates are bonded before the at least one cut is formed therein.

2. Method according to claim 1 including the step of making at least one cut in an external face of the second substrate, the cut being of sufficient depth to intersect one or more of said channels such that only the required interconnections are made by the at least one cut.

3. Method according to claim 2 including the steps of a) forming at least one flow path in a third substrate and b) joining the third substrate to the first and second substrates.

4. Method according to any preceding claim wherein the at least one cut formed in the first substrate and the at least one cut formed in the second substrate are off-set.

5. Method according to any preceding claim wherein the at least one cut is formed substantially perpendicular to the plane of the substrate.

6. Method according to any preceding claim wherein the cuts are formed by sawing.

7. Method according to any preceding claim wherein the cuts are formed by mechanical milling.

8. Method according to any preceding claim wherein the cuts are formed by laser ablation.

AMENDED SHEET

PCT 20.03.00

9. Method according to any preceding claim wherein the cuts are formed by photolithography.

10. Method according to any preceding claim wherein the cuts are formed by chemical etching.

11. Apparatus for transporting at least one fluid, the apparatus including at least a first substrate and a second substrate which have portions removed therefrom, so as to define at least one channel, the at least one channel being interconnected according to the method of claims 1 to 10.

12. Apparatus according to claim 11 further including a third substrate situated between the first and second substrates.

13. Apparatus according to claim 11 further including a third substrate situated adjacent the second substrate, the third substrate having portions removed therefrom so as to define at least one channel.

14. Apparatus according to claim 11 wherein the first substrate is glass.

15. Apparatus according to claim 11 wherein the second substrate is silicon.

16. Apparatus according to claim 12 wherein the third substrate is a mesh.

17. Apparatus according to claim 12 wherein the third substrate includes a polymer.

18. Apparatus according to claim 13 wherein the third substrate is glass.

19. Apparatus according to any of claims 11 to 18 wherein the substrate is a square approximately 5×10^{-2} m x 5×10^{-2} m.

20. Apparatus according to claim 11 wherein the channels are substantially straight.

21. Apparatus according to claim 11 wherein the channels are substantially curved.

22. Apparatus according to claim 11 wherein the channels are between 1×10^{-2} m and 5×10^{-2} m in length.

23. Method of connecting channels formed in at least one substrate by making at least one cut in at least one external face of said substrate, the cut being of sufficient

IN 20.03.00

depth to intersect one or more of said channels such that only the required interconnections are made by each cut.

24. A micro-fluidic device incorporating the apparatus as claimed in claims 11 to 22.

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

To:

HARRISON GODDARD FOOTE
Tower House
Merrion Way
Leeds LS2 8PA
ROYAUME-UNI

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

Date of mailing (day/month/year) 27 July 2000 (27.07.00)	
Applicant's or agent's file reference P.Q. 12,768	**IMPORTANT NOTIFICATION**
International application No. PCT/GB99/00018	**International filing date** (day/month/year) 05 January 1999 (05.01.99)

1. The following indications appeared on record concerning:

[] the applicant [] the inventor [X] the agent [] the common representative

Name and Address	State of Nationality	State of Residence
WALKER, Neville, Daniel, Alan QED I.P. Services Limited Dawley Road Hayes Middlesex UB3 1HH United Kingdom		
	Telephone No. 0181 848 6692	
	Facsimile No. 0181 848 6469	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [] the name [] the address [] the nationality [] the residence

Name and Address	State of Nationality	State of Residence
HARRISON GODDARD FOOTE Tower House Merrion Way Leeds LS2 8PA United Kingdom		
	Telephone No. 44 113 290 1400	
	Facsimile No. 44 113 244 2829	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[] the International Searching Authority
[X] the International Preliminary Examining Authority
[] the designated Offices concerned
[X] the elected Offices concerned
[] other:

The International Bureau of WIPO **34, chemin des Col mbettes** **1211 Geneva 20, Switzerland**	Authorized officer R. Chrem
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994) 003436212

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 27 August 1999 (27.08.99)	
International application No. PCT/GB99/00018	**Applicant's or agent's file reference** P.Q. 12,768
International filing date (day/month/year) 05 January 1999 (05.01.99)	**Priority date** (day/month/year) 06 January 1998 (06.01.98)
Applicant SHAW, John, Edward, Andrew et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

26 July 1999 (26.07.99)

[] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Lazar Joseph Panakal

Telephone No.: (41-22) 338.83.38

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
B01J 19/00, F28F 27/02

A1

(11) International Publication Number: WO 99/34909

(43) International Publication Date: 15 July 1999 (15.07.99)

(21) International Application Number: PCT/GB99/00018

(22) International Filing Date: 5 January 1999 (05.01.99)

(30) Priority Data:
9800220.7 6 January 1998 (06.01.98) GB

(71) Applicant *(for all designated States except US)*: CENTRAL RESEARCH LABORATORIES LIMITED [GB/GB]; Dawley Road, Hayes, Middlesex UB3 1HH (GB).

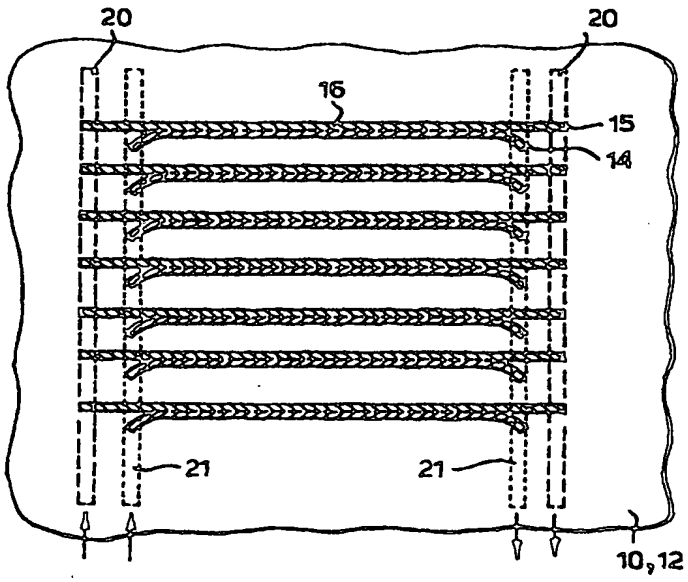
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: SHAW, John, Edward, Andrew [GB/GB]; 45 Colne Avenue, West Drayton, Middlesex UB7 7AL (GB). TURNER, Chris [GB/GB]; 56 Waterside, Uxbridge, Middlesex UB8 2LQ (GB).

(74) Agent: WALKER, Neville, Daniel, Alan; QED I.P. Services Limited, Dawley Road, Hayes, Middlesex UB3 1HH (GB).

(81) Designated States: AU, BR, CA, IL, JP, RU, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: METHOD OF FORMING INTERCONNECTIONS BETWEEN CHANNELS AND CHAMBERS



(57) Abstract

A method of forming interconnections between channels and/or chambers for use in a micro–fluidic device. Two planar substrates (10, 12) (usually glass and silicon respectively) having etched channels (14, 15) are bonded together to form volmes (16) where the channels (14, 15) overlap. A manifolding cut (20) is then made through the glass to intersect channels (15) in the silicon layer. Another cut (21) is made through the glass, intersecting glass channels (14) only. An organic solution is passed into cut (20), and flows through silicon channels (15). An aqueous solution is passed into cut (21), and flows through glass channels (14). The solutions meet in the region (16), where matter is transferred from one solution to the other.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/GB 99/00018

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 B01J19/00 F28F27/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 B01J F28F F15C F28D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 195 11 603 A (SCHWESINGER) 2 October 1996 see column 4, line 49 - line 55 see column 6, line 67 - column 7, line 14 see figures 2,10,11	1,2,4, 6-13,16, 17,21-25
X	WO 95 05008 A (WILLEKE) 16 February 1995 see abstract see page 16, paragraph 2 - page 17, paragraph 2 see figure 8	1,6-10, 12

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 April 1999	06/05/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	SLEIGHTHOLME, G

1

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 00442 A (UNIV WASHINGTON) 3 January 1997 see page 27, line 1 - line 23 see page 44, line 24 - page 45, line 6 see figures 5,6	1,6,11
A	US 5 099 311 A (BONDE) 24 March 1992 see column 4, line 58 - line 64 see column 5, line 28 - line 45 see figures 2,3,6,7	1,2,13, 21,24,25
A	US 5 681 484 A (CHERUKURI) 28 October 1997 see column 13, line 61 - column 14, line 18; figures 11A-D	1,13,25
A	US 5 152 060 A (BICHLER) 6 October 1992 see abstract; figure 2	8,9
A	WO 96 12541 A (BULL) 2 May 1996 cited in the application see abstract; figure 1A	23

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 99/00018

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 19511603 A	02-10-1996	WO 9630113 A	03-10-1996
		EP 0879083 A	25-11-1998
WO 9505008 A	16-02-1995	DE 4426347 A	02-02-1995
		EP 0742959 A	20-11-1996
		JP 9501268 T	04-02-1997
		US 5704992 A	06-01-1998
WO 9700442 A	03-01-1997	AU 6541596 A	15-01-1997
		CA 2222126 A	03-01-1997
		EP 0839318 A	06-05-1998
US 5099311 A	24-03-1992	NONE	
US 5681484 A	28-10-1997	US 5585069 A	17-12-1996
		AU 4152396 A	06-06-1996
		AU 4233796 A	06-06-1996
		CA 2204912 A	23-05-1996
		CA 2205066 A	23-05-1996
		EP 0791238 A	27-08-1997
		EP 0808456 A	26-11-1997
		JP 11500602 T	19-01-1999
		WO 9615450 A	23-05-1996
		WO 9615576 A	23-05-1996
		US 5643738 A	01-07-1997
		US 5593838 A	14-01-1997
		US 5846396 A	08-12-1998
		US 5755942 A	26-05-1998
		US 5863708 A	26-01-1999
		US 5858804 A	12-01-1999
US 5152060 A	06-10-1992	DE 3709278 A	29-09-1988
		AT 75980 T	15-05-1992
		WO 8806941 A	22-09-1988
		EP 0391895 A	17-10-1990
		JP 2854309 B	03-02-1999
		JP 3500861 T	28-02-1991
		US 5249359 A	05-10-1993
WO 9612541 A	02-05-1996	AT 175362 T	15-01-1999
		AU 695237 B	13-08-1998
		AU 3703095 A	15-05-1996
		AU 699883 B	17-12-1998
		AU 3703195 A	15-05-1996
		CA 2203282 A	02-05-1996
		CA 2203283 A	02-05-1996
		DE 69507157 D	18-02-1999
		EP 0787029 A	06-08-1997
		EP 0790849 A	27-08-1997
		WO 9612540 A	02-05-1996
		JP 10507406 T	21-07-1998
		JP 10507962 T	04-08-1998

Method of Forming Interconnections between Channels and Chambers

This invention relates to a method of forming interconnections between channels and chambers, and more particularly to such a method for use in micro-engineered fluidic devices.

Micro-engineered devices may be used to transport and control fluid flow. Such devices may be used in a variety of applications including chemical and physical analysis, chemical processing, and heat transfer. Micro-engineered fluidic devices for use in the transport of immiscible fluids are described in International Patent Applications WO 96/12540 and WO 96/12541.

The advantages of using micro-fluidic devices containing channels and chambers are:

1. Only small sample sizes are needed for analysis; and
2. Transport distances for chemical processing of fluids are usually small; and
3. Heat transfer is improved.

Channels and chambers are usually formed on planar substrates, and are hereinafter referred to as "channels". There is a need for the linking of individual channels for applications which require a high fluid throughput, as fluid flow in conventional micro-engineered devices may be very low. Channels may be produced by forming grooves or depressions on one or more faces of a substrate. Such substrates may then be bonded together. Vias may also be formed in the substrate, and may connect to channels formed therein.

A number of known methods are used to form channels on the faces of planar substrates. These include:-

1. Etching using mask patterns defined by a lithographic process such as photolithography, screen printing, or direct writing; or
2. Cutting, milling, or drilling substrates by spark erosion, or laser ablation; or
3. Deposition or building up of layers on substrates according to patterns defined by lithographic processes; or
4. Electroplating through printing or photo-defined mask layers, including the use of X-ray lithography, as in LIGA (Lithographic Galvanoformung Abformung); or
5. The build up of substrates by bonding lamina, some of which may be cut to define a pattern of grooves or depressions; or
6. Mould replication or stamping of substrates defined by any of the above processes.

A common process is to form a fluid-handling micro-engineered device by anodic bonding of glass and silicon substrates having channels formed on one or both of the substrates.

Arrangements are known in the prior art for forming external connections and interconnections in substrates. External connections to channels are achieved by vias passing through to external faces of substrates, or by having channels extend to the edge of one or more of the substrates. Vias may be formed through one or more of the substrates to form interconnections between the channels. For simple devices with few external connections it is adequate to employ these methods. Methods for connecting capillaries to channels extending to the edge of a device composed of one or more substrates are described in UK Patent Application No. 9625491.7.

It is well established for electronic devices, that minimisation of the number of external input/output connections to arrays of charge pathways on a single substrate requires the routing of connections perpendicular to the substrate plane. This is achieved through the use of vias. The same topological requirements apply to fluidic devices where various feed and exit pathways connecting to channels should not intersect with each other, other than at the channel itself. For complex devices, a large number of external connections may be required.

Devices with vias and connections in multiple planar substrates correspond to the topological forms used to provide the dense connectivity required for integrated electronic devices. Within such electronic devices, charge pathways are defined in solid, self-supporting materials. The layers of material are usually thin enough to enable sufficient planarity to be maintained, allowing deposition, photolithography and etching to be carried out with good results.

In micro-fluidic devices, channels and vias are generally of larger dimensions than corresponding pathways and vias in integrated electronic devices. Channels are not self-supporting, as are the pathways in integrated electronic devices, because the formation of a channel, or a via, involves removing a volume of the substrate. Manufacture of channels and vias therefore contributes to fragility of the device, lowering yield during fabrication. This is especially true for vias, as they are formed perpendicular to the substrate plane. In addition, the difficulty of etching high aspect ratio vias (that is, a via whose length through the substrate is greater than its width) requires that the lateral dimensions of vias in the substrate plane are similar to (or often greater than) the

thickness of the substrate in which they are formed. This last constraint may be overcome by use of techniques such as laser ablation or trench etching, but such techniques are expensive and not widely available.

It is particularly difficult to photo-define and etch mask layers within the area of a narrow channel formed by a previous fabrication sequence in a micro-fluidic device. This constraint dictates that channels for micro-fluidic devices fabricated by conventional procedures are produced with a relatively low density. This is especially true for vias. Consequently, the cost per device is increased.

Typically, the density of channels formed on a substrate cannot be greater than that indicated in Figure 1, where *a* is of the order of the thickness of the substrate. This applies to micro-contactor arrays with channels connecting to vias produced by anisotropic or isotropic etching of a substrate. It is therefore desirable that a way of allowing interconnection and manifolding of channels is found, without the problems of low density of channels, fragility of the device, or poor manufacturing yield.

An aim of the invention is to overcome the aforementioned problems by providing a method of constructing interconnections and/or manifolds in substrates, particularly, but not exclusively, for use in micro-fluidic devices.

According to a first aspect of the invention there is provided a method of connecting channels formed in at least one substrate by making at least one cut in at least one external face of said substrate, the cut being of sufficient depth to intersect one or more of said channels such that only the required interconnections are made by each cut.

According to a second aspect of the invention there is provided a method of connecting channels including a) forming at least one flow path in a first substrate; b) forming at least one flow path in a second substrate; c) contacting the first and second substrates to form at least one channel; and d) forming at least one cut in an external face of the first substrate, the cut being of sufficient depth to intersect one or more of the channels such that, in use, a fluid passing along a fluid pathway defined by the cut may pass into the or each channel.

Preferably the substrates are bonded before the cuts are formed therein, in order to maintain the physical integrity of a device incorporating the invention. The substrates

may be bonded via anodic or thermal bonding, or by gluing using suitable adhesives such as epoxy, acrylic, or UV curing adhesives.

The method may also include the step of making at least one cut in an external face of the second substrate, the cut being of sufficient depth to intersect one or more of said channels such that only the required interconnections are made by the at least one cut.

The method preferably includes the steps of a) forming at least one flow path in a third substrate and b) joining the third substrate to the first and second substrates.

Advantageously the at least one cut formed in the first substrate and the at least one cut formed in the second substrate are off-set in order to maintain the physical integrity of a device incorporating the invention.

The at least one cut is preferably formed substantially perpendicular to the plane of the substrate.

Cuts may be produced by micro-engineering sawing methods, which can be controlled to within 10μm. Alternatively, it is possible to use mechanical milling, as long as the equipment used is of relatively high precision. Laser ablation, or photolithography and chemical etching may also be applied to produce the manifolding channels. Although, in general, mechanical cutting or milling systems are preferred.

According to a further aspect of the invention there is provided an apparatus for transporting at least one fluid, the apparatus including at least a first substrate and a second substrate which have portions removed therefrom, so as to define at least one channel, the at least one channel being interconnected according to the aforedescribed method.

Preferably the apparatus further includes a third substrate. The third substrate may be situated between the first and second substrates, or adjacent the second substrate.

Preferably the first substrate is glass.

Preferably the second substrate is silicon.

If the third substrate is situated between the first and second substrates, the third substrate is preferably a mesh of, for example, copper or steel. Alternatively, it may include a polymer. The third substrate is preferably between 1 and 10 micrometres thick.

Where the third substrate is situated adjacent the first or the second substrates, the third substrate is preferably glass. The third substrate may have portions removed therefrom so as to define at least one channel.

Preferably the substrate is a square approximately 5×10^{-2} m by 5×10^{-2} m.

The channels may be substantially straight or curved.

Preferably the channels are between 1×10^{-2} m and 5×10^{-2} m in length.

The invention may be incorporated into a micro-fluidic (or other) device.

Fluids used within the device may either be miscible or immiscible. Aqueous and/or organic material may be used within the device.

Preferred embodiments of the invention will now be described, by way of example only, with reference to the accompanying Figures, wherein:-

Figure 1 shows a plan view of channels and chambers formed on a substrate, known in the prior art;

Figure 2 shows a cross-section of two planar substrates containing channels;

Figures 3a and 3b show a cross-section of two bonded planar substrates containing channels;

Figures 4a and 4b show a plan view of two bonded planar substrates shown in Figure 3;

Figures 5a and 5b show a cross-section along line v-v' of Figure 4a and 4b respectively, where manifold cuts have been made in the substrates, in accordance with the present invention;

Figures 6a and 6b show a plan view of two bonded planar substrates shown in Figures 3a to 5a and Figures 3b to 5b respectively, where manifold cuts have been made in the substrates;

Figure 7 shows a cross-section of two bonded planar substrates along line v-v' of Figure 6a;

Figure 8 shows a cross-section of a further embodiment of the invention showing two bonded planar substrates containing channels, where manifold cuts have been made in one substrate only;

Figure 9 shows an oblique view of the embodiment shown in Figure 8;

Figure 10 shows an oblique view of a further embodiment of the present invention;

Figure 11 shows a plan view of a device incorporating the invention;

Figure 12 shows a further embodiment of the invention showing two bonded planar substrates containing two sets of channels, where manifold cuts have been made to link one set of channels only;

Figure 13a shows a cross-section of a laminated structure;

Figure 13b shows a cross-section of a laminated structure having chambers formed therein;

Figure 14a is a plan view of the laminated structures of Figure 13 showing the positions of manifold cuts;

Figure 14b is a plan view of a laminated structure, showing the positions of manifold cuts at an angle to one another; and

Figures 15a to 15d show plan views of the laminated structures of Figure 13 having manifold cuts.

Referring to Figure 2, channels 14 are formed on a surface of planar substrate 10, which in this case is glass. Channels 15 are also formed on a surface of planar substrate 12, which is this case is silicon. Vias needed to interconnect the individual channels are not formed at this stage. Substrate layers 10 and 12 are then bonded together to form channels 14 and 15, as shown in Figures 3a and 3b. The substrates may be bonded using epoxy adhesive such as EpoTek™ 353 ND, or UV curing acrylic adhesive such as Norland Optical adhesive type 81.

From Figures 3a and 4a, it can be seen that the channels 14 in substrate 10 overlap channels 15 in substrate 12 to provide regions where fluids flowing in the respective channels 14, 15 contact at an interface 18. In an alternative embodiment, however, channels 14 and 15 do not overlap and there is no interface between the channels. This embodiment is shown in Figures 3b and 4b.

Interconnections or manifolds to groups or arrays of channels 14 or 15 are formed by cuts 19, 20 made into one or more of the external faces of the bonded substrates 10 and 12, as illustrated by Figures 5 and 6. Figures 5a and 6a show bonded substrates where channels 14 and 15 overlap to form an interface 18, whereas Figures 5b and 6b shows bonded substrates where channels 14 and 15 do not overlap. The position and depth of these cuts is such that only required connections to respective channels 14 or 15 are made by each cut. Cuts 20 made to substrate 10 should not extend deeply into substrate 12 so that the physical integrity of the assembled device is maintained. For channels which are 40

micrometres in depth, cuts made to an accuracy of approximately 10 micrometres are adequate.

Two methods for forming manifolds will now be discussed. Figure 7 shows a first embodiment, where the manifolds 19 and 20 are cut in both substrate layers 12 and 10 respectively, and are offset. Cut 19 is made through substrate 12 only, to intersect channels 15. Cut 20 is made through substrate 10 only, to intersect channels 14. Figure 8 shows a further embodiment of the invention, where manifolds 20 and 21 are cut in the same substrate 10. Cut 20 is made through substrate 10, and is deep enough so that it intersects with channels 15 in substrate 12. Cut 21 is also made through substrate 10, but its depth is less than that of cut 20, so that it only intersects with channels 14 in substrate 10.

Where both substrates contain cuts, as in Figure 7, the cuts should be offset, or positioned so as not to weaken the device. Formation of the interconnections generally involves at least some of the cuts through a substrate sufficiently to intersect the channels 14, 15 to be linked, and not continuing through to the interface 18 between bonded substrates 10, 12.

Where one of the substrates is transparent (substrate 10 in this case), it is advantageous to form all the manifold cuts through the transparent substrate, as in Figures 8 and 9. This allows more precise alignment of the cuts with the channels on further substrate layers.

The examples shown diagrammatically in Figures 2 to 9 are that of a micro-contactor. Similar steps may be taken to form other micro-fluidic devices from various planar substrates, provided that such substrates can be bonded and accurately cut. For example, in Figure 10, substrate 11 having manifold cuts 22, is bonded to substrates 10 and 12, which themselves contain manifold cuts 19 and 20. The resulting device has an increased manifold cross-section, and flow capacity is increased.

The depth of cuts 19 is not critical, as long as the cuts are deep enough to intersect with the channel which is to be connected with the cut, and does not pass far enough into a further substrate to weaken the assembly. For a micro-contactor, it is required that the manifolding connections do not cross the interface between the channels 14 and 15. If manifolding connections cross the interface, fluids tend to mix, and establishment of a stable fluid interface position is prevented. This is important for manifolding positions 21 shown in Figure 8, where pairs of contactor channels 14 and 15 intersect the plane of the manifold cut. Here it must be ensured that the depth of the cut is limited to a range

sufficient to intersect predetermined channels 14 and 15 etched into the substrate being cut, while not allowing the cut to reach the interface between the substrates.

The restriction on the depth of manifold cuts applies to structures other than micro-contactors.

The method of the invention may also be applied to any fluidic structure where it is required that channels to be interconnected may not intersect another set of channels. Here, channels 14 and 15 are formed in a layer of substrate 10. Channels 14 are deeper than channels 15, so that manifolding cuts made to connect channels 14 do not link channels 15. An example of this is shown in Figure 12. This concept may be of use in a heat exchanger, for example. In addition to channels 14, 15 carrying fluids, the channels may be an electronically conducting conduit, or a light guide or other structure situated between the channels to be connected, but which must remain isolated from the manifolding.

Figures 13a and 13b show a cross-section of a bonded, layered structure in which manifold cuts have not yet been formed. The bonded structure shown in Figure 13a includes a thin middle layer 30 of substrate, the central portions of which are bonded to an upper substrate layer 32a, and a lower substrate layer 32b. The outer regions of one side of layer 30 are bonded to a first substrate layer 10, and the outer regions of the other side of layer 30 are bonded to a second substrate layer 12. Material 32 (which is in contact with the central portions of layer 30) can be dissolved or melted out at a later stage. Layers 32a,b may, for example, contain a polymer or a polymer/wax mix, a metal such as copper, or an alloy such as steel which may be in the form of a mesh. The layers of material 32a and 32b are further bonded to respective layers of substrate 10 and 12, such that when the material 32 is removed, respective chambers 34a and 34b are formed in the substrate layers 10 and 12.

The laminated structure may, alternatively, be formed by bonding the outer regions of one side of layer 30 to a first substrate layer 10, and on the other by a second substrate layer 12, the substrate layers 10 and 12 having cut-away portions so as to form chambers 34a,b without the need for layers 32a,b. Such a laminated structure is shown in Figure 13b. This structure provides less support than that shown in Figure 13a, but the outer uncut layers 10,12 provide physical stability to the whole structure during assembly and bonding, thus reducing distortion of the layered structure.

Figure 14a shows a plan view of the laminated structures of Figures 13a and 13b, indicating the positions of the manifolding cuts 19 and 20. In this structure, the manifolding cuts 19 and 20 run parallel to each other. However, the manifolding cuts may be made so that they are at an angle to each other, as shown in Figure 14b. The angle should be high enough in order that the device is not weakened.

Figures 15a to 15d show cross-sections of the laminated structures of Figures 13a and 13b having various manifolding cuts formed therein. Figure 15a shows a laminated structure having manifolding cuts 20 and 19 formed in substrates 10 and 12 respectively. In this case, the cuts are made as far as layers 32a,b. The material 32 is then removed (as previously discussed) in order to form chambers 34a,b which are connected to channels 20 and 19. Cuts 19 and 20 are offset so as not to weaken the device. Figure 15c shows a layered structure having manifolding cuts 20 and 21 made in the external face of substrate 10. Cut 20 extends to the upper layer 32a, and cut 21 extends (via layer 30) to the lower layer 32b. When the material of layers 32a and 32b is removed, respective chambers 34a and 34b are formed. Chambers 34a and 34b are linked via manifolding cuts 20 and 21, respectively.

Figure 11 shows a schematic plan view of a device having a number of channels 14, 15 and manifold cuts 20, 21. The structure of the device is the same as that shown in Figures 8 and 9. Organic material passes through channels 15 formed in silicon substrate 12 via manifolding cuts 20. Cuts 20 pass through the glass substrate 10 and silicon substrate 12 in order to intersect channels 15 formed in the silicon substrate 12. Aqueous material flows in channels 14 formed in glass substrate 10 via manifolding cuts 21. Here the organic material used in a mixture of Xylene and TBP (tributylphosphate) containing dissolved iron ions (Fe^{3+}), and the aqueous material is hydrochloric acid. Where channels 14 and 15 meet, the aqueous and organic materials come into contact. There is a transfer of iron ions from the organic material to the aqueous material. This reaction is an example of a liquid-liquid solvent extraction process and is used, for example, in the pharmaceutical and nuclear industries. The organic and aqueous materials then exit from the device.

Devices produced using this method may have 120 micro-contactors of length 14mm, formed in an area of substrate 50 mm square. This is approximately ten times the density of channels achievable using past methods of etching through a substrate and using structures such as those shown in Figure 1 having vias 2 and channels 4. Fluid flow and transfer rates for devices produced using the present invention have improved by a factor of 120 over the methods in the prior art.

In summary, devices manufactured according to the method of forming interconnections of channels as herein described has the following advantages:

1. better utilisation of space/higher packing density of channels than other methods;
2. improved yield as the channels formed in one substrate are supported by another substrate;
3. improved yield due to the substrates being less likely to break during the bonding process than using other methods; and
4. improved strength of the assembled device.

The invention has been described by way of a number of embodiments and it will be appreciated that variation may be made to these embodiments without departing from the scope of the invention.

Claims

1. Method of connecting channels formed in at least one substrate by making at least one cut in at least one external face of said substrate, the cut being of sufficient depth to intersect one or more of said channels such that only the required interconnections are made by each cut.

2. Method of connecting channels including a) forming at least one flow path in a first substrate; b) forming at least one flow path in a second substrate; c) contacting the first and second substrates to form at least one channel; and d) forming at least one cut in an external face of the first substrate, the cut being of sufficient depth to intersect one or more of the channels such that, in use, a fluid passing along a fluid pathway defined by the cut may pass into the or each channel.

3. Method according to claim 2 wherein substrates are bonded before the cuts are formed therein.

4. Method according to claims 2 or 3 including the step of making at least one cut in an external face of the second substrate, the cut being of sufficient depth to intersect one or more of said channels such that only the required interconnections are made by the at least one cut.

5. Method according to claim 4 including the steps of a) forming at least one flow path in a third substrate and b) joining the third substrate to the first and second substrates.

6. Method according to any preceding claim wherein the at least one cut formed in the first substrate and the at least one cut formed in the second substrate are off-set.

7. Method according to any preceding claim wherein the at least one cut is formed substantially perpendicular to the plane of the substrate.

8. Method according to any preceding claim wherein the cuts are formed by sawing.

9. Method according to any preceding claim wherein the cuts are formed by mechanical milling.

10.Method according to any preceding claim wherein the cuts are formed by laser ablation.

11. Method according to any preceding claim wherein the cuts are formed by photolithography.

12. Method according to any preceding claim wherein the cuts are formed by chemical etching.

13. Apparatus for transporting at least one fluid, the apparatus including at least a first substrate and a second substrate which have portions removed therefrom, so as to define at least one channel, the at least one channel being interconnected according to the method of claims 1 to 12.

14. Apparatus according to claim 13 further including a third substrate situated between the first and second substrates.

15. Apparatus according to claim 13 further including a third substrate situated adjacent the second substrate, the third substrate having portions removed therefrom so as to define at least one channel.

16. Apparatus according to claim 13 wherein the first substrate is glass.

17. Apparatus according to claim 13 wherein the second substrate is silicon.

18. Apparatus according to claim 14 wherein the third substrate is a mesh.

19. Apparatus according to claim 14 wherein the third substrate includes a polymer.

20. Apparatus according to claim 15 wherein the third substrate is glass.

21. Apparatus according to any of claims 13 to 20 wherein the substrate is a square approximately 5×10^{-2} m x 5×10^{-2} m.

22. Apparatus according to claim 13 wherein the channels are substantially straight.

23. Apparatus according to claim 13 wherein the channels are substantially curved.

24. Apparatus according to claim 13 wherein the channels are between 1 x 10^{-2} m and 5 x 10^{-2} m in length.

25. A micro-fluidic device incorporating the apparatus as claimed in claims 13 to 24.

26. Method as substantially described herein with reference to the Figures.

27. Apparatus as substantially described herein with reference to the Figures.

Fig.1.

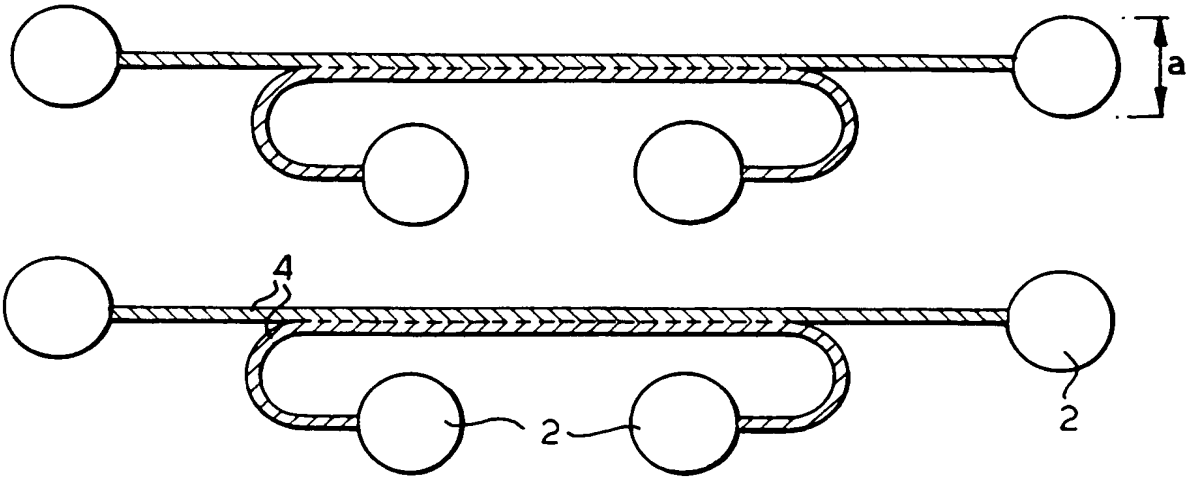


Fig.2.

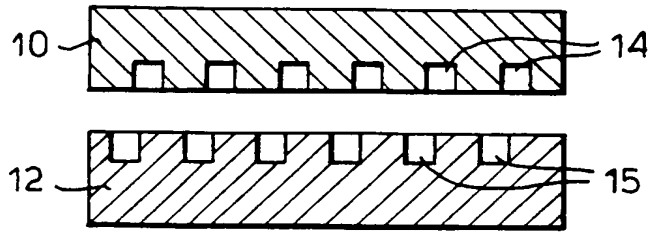


Fig.3a.

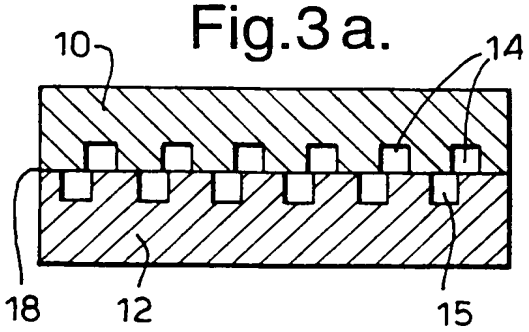


Fig.3b.

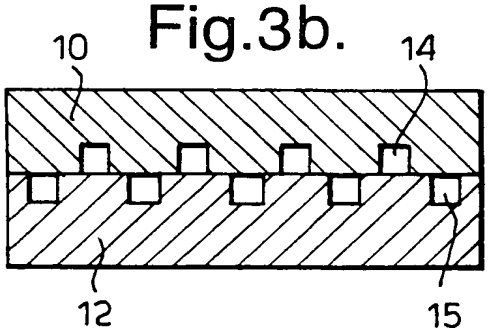


Fig.4a.

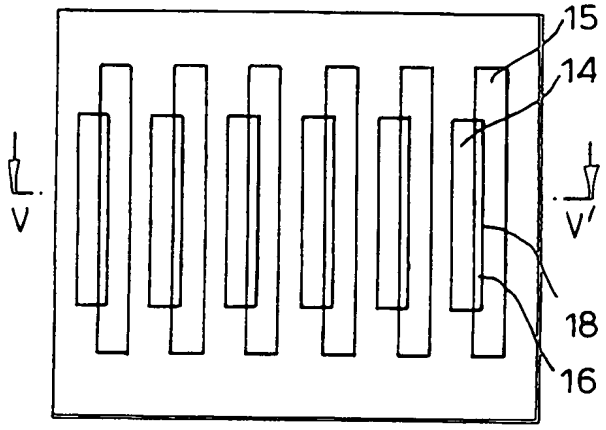


Fig.4b.

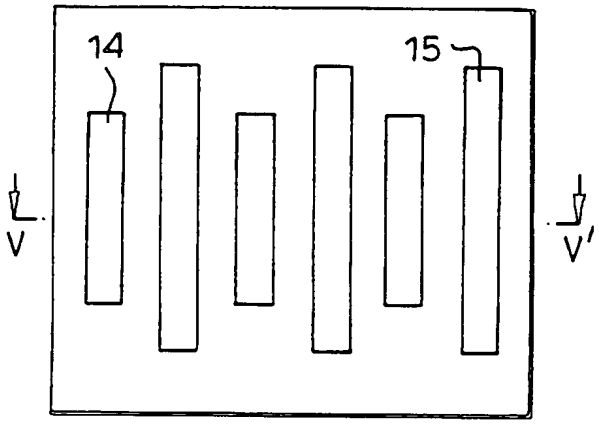


Fig.5a.

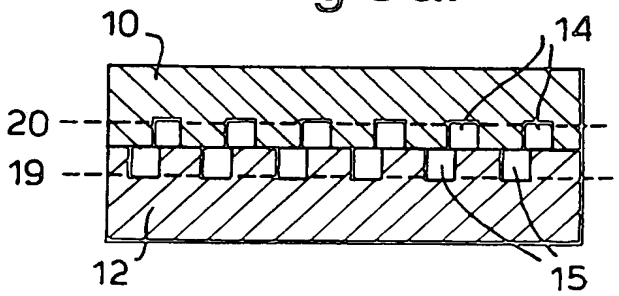


Fig.5b.

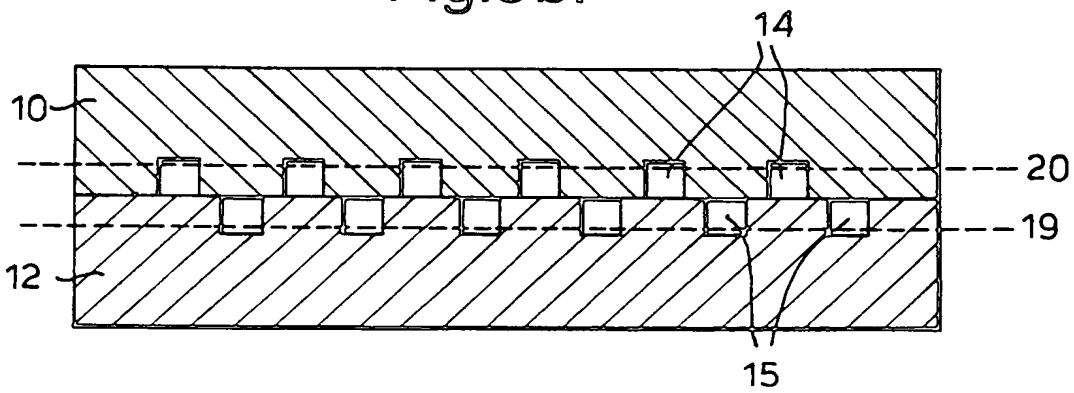


Fig.6a.

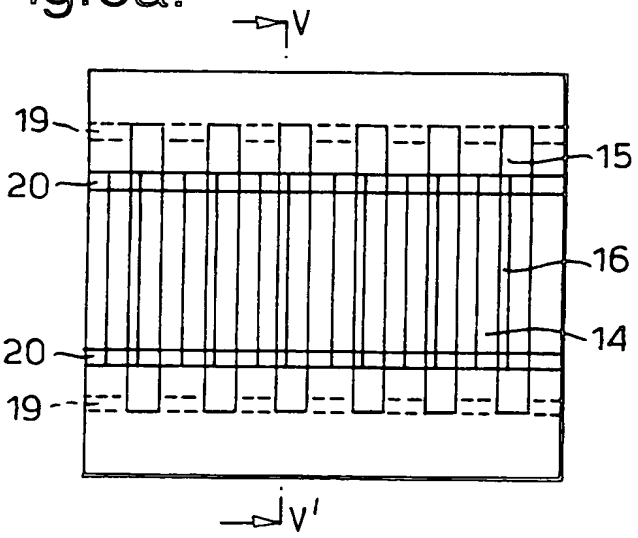


Fig.6b.

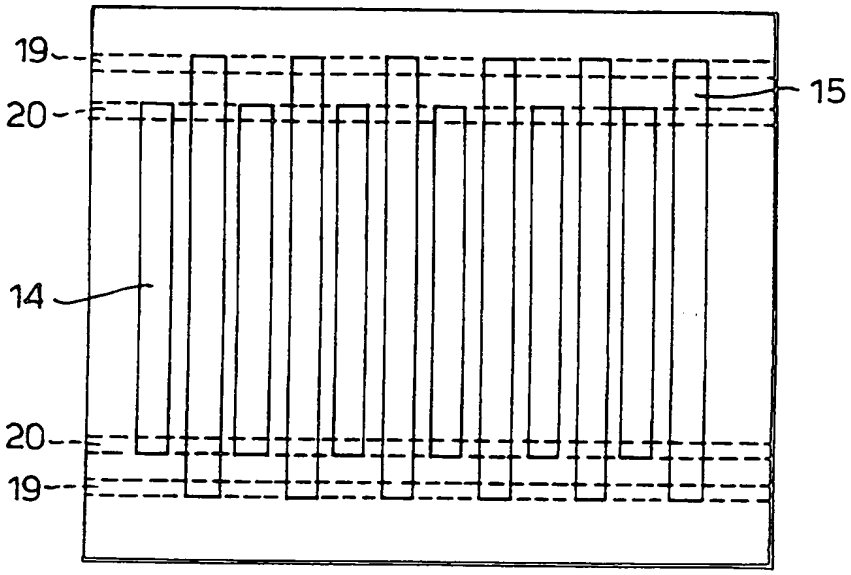


Fig.7.

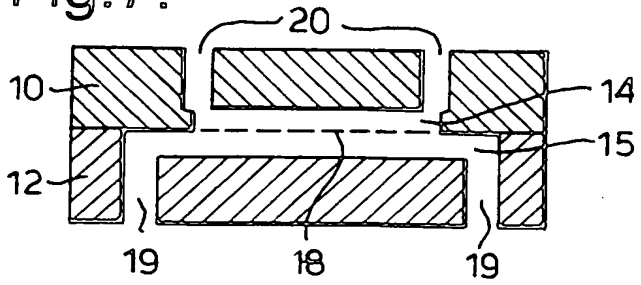


Fig.8.

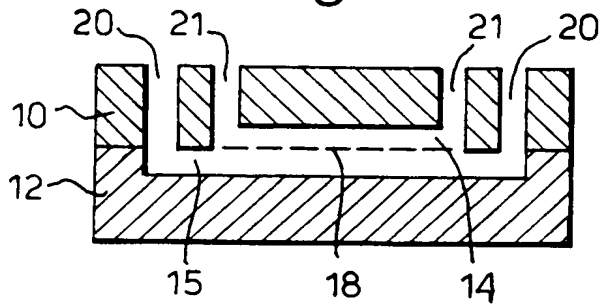


Fig.9.

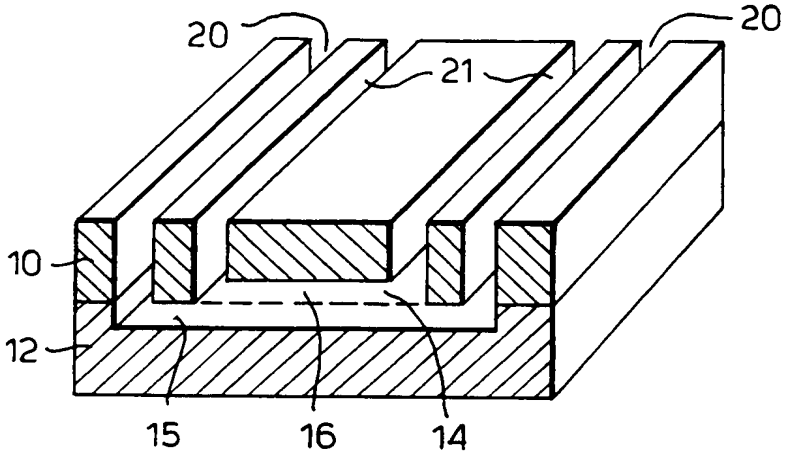


Fig.10.

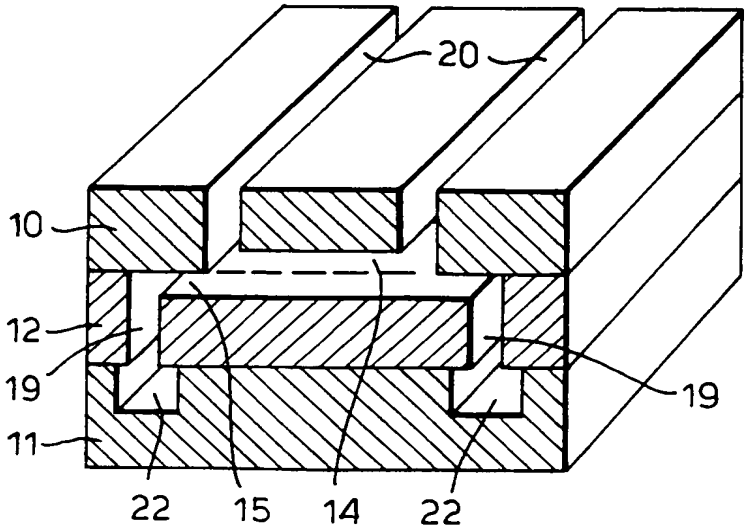


Fig.11.

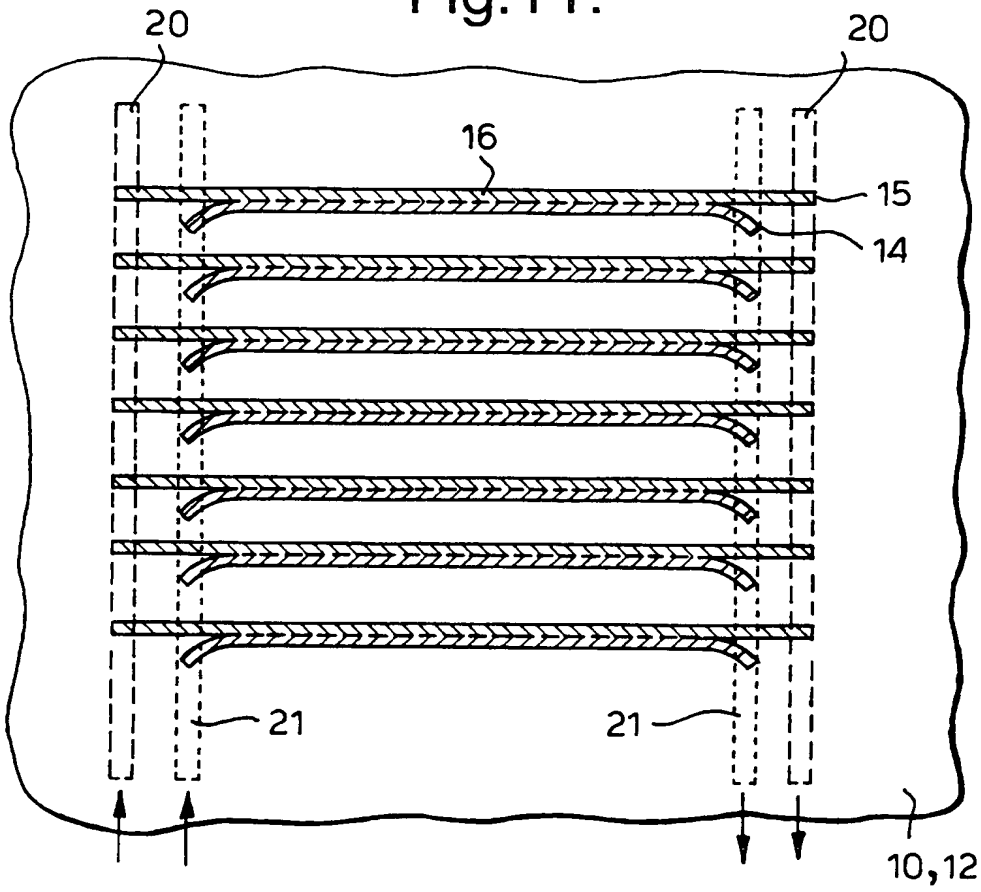


Fig.12.

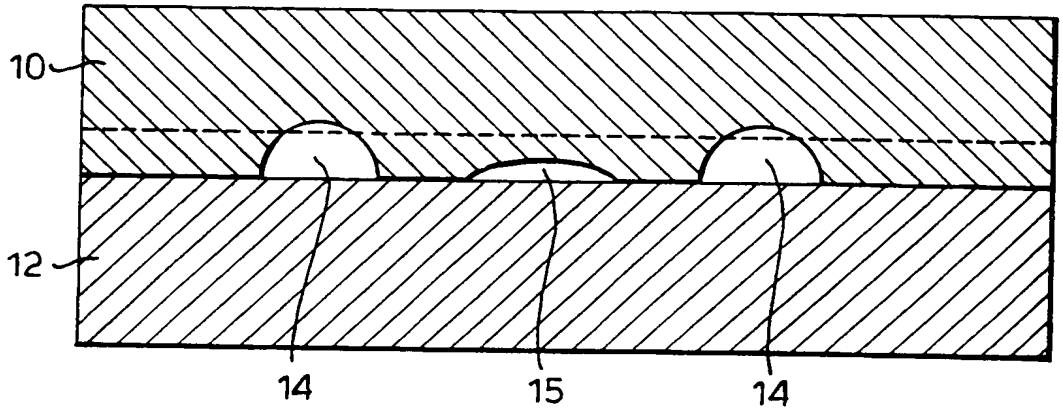


Fig.13a.

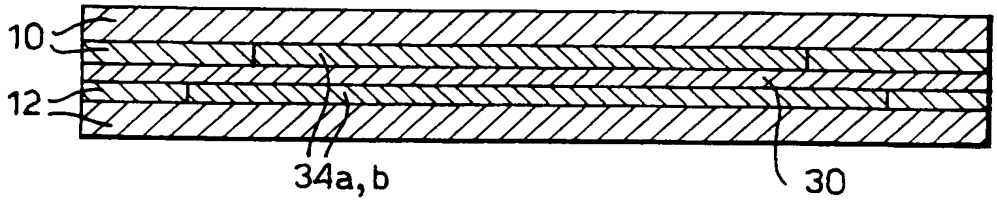


Fig.13b.

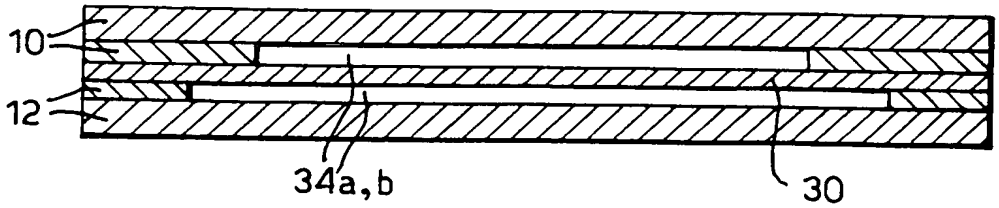


Fig.14a.

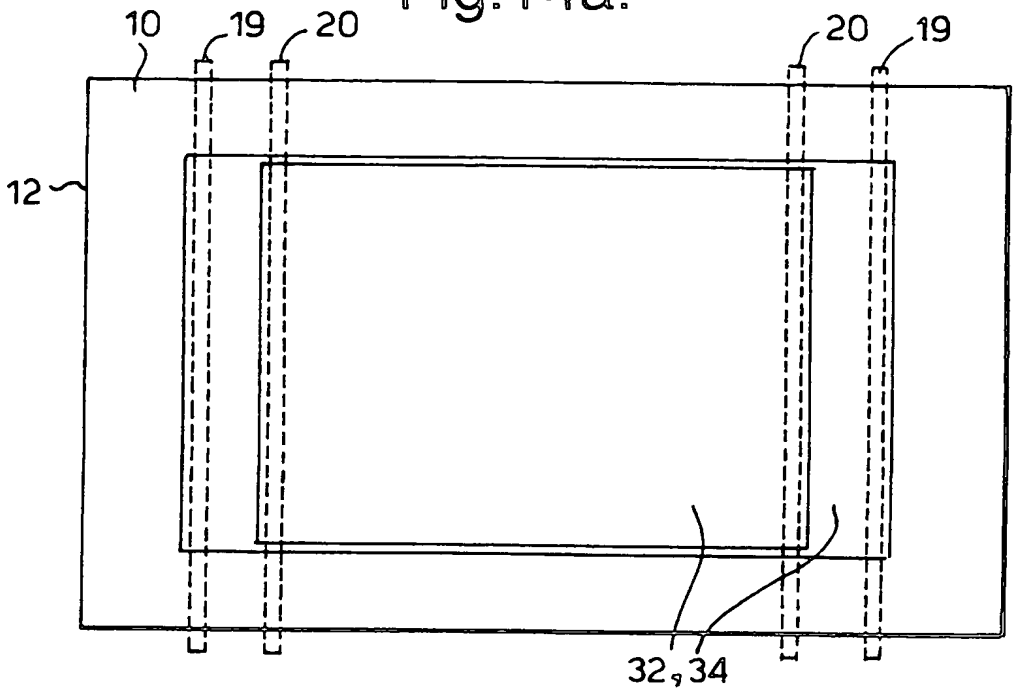


Fig.14b.

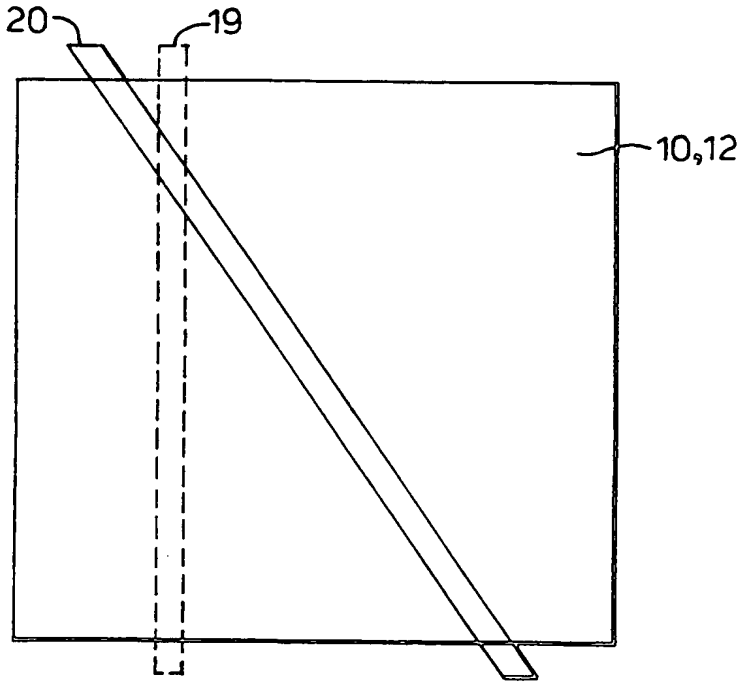


Fig.15a.

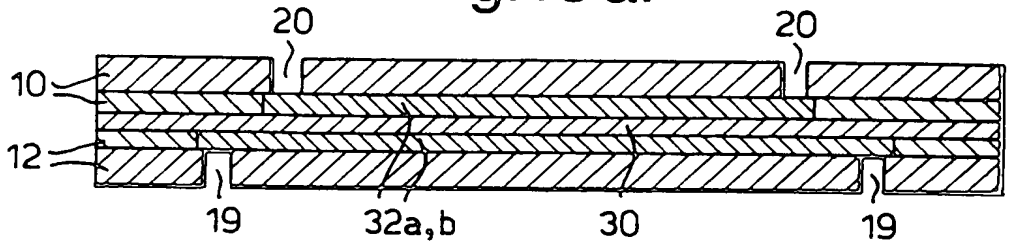


Fig.15b.

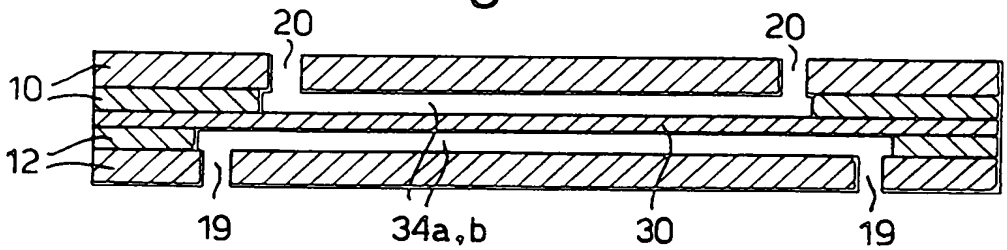


Fig.15c.

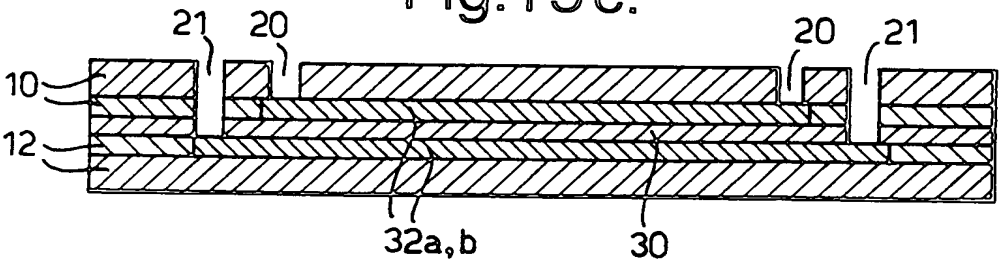
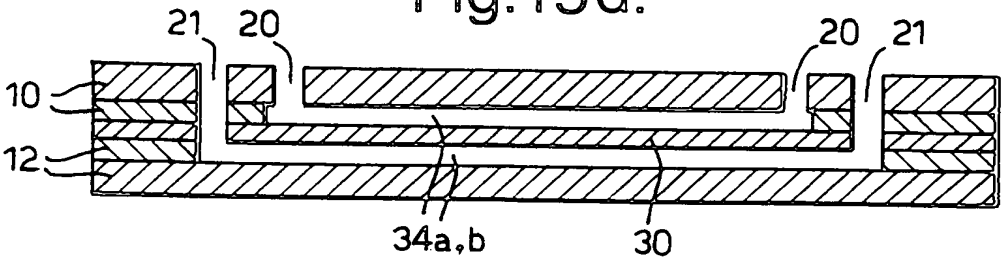


Fig.15d.



INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/GB 99/00018

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 B01J19/00 F28F27/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 B01J F28F F15C F28D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 195 11 603 A (SCHWESINGER) 2 October 1996 see column 4, line 49 - line 55 see column 6, line 67 - column 7, line 14 see figures 2,10,11 ---	1,2,4, 6-13,16, 17,21-25
X	WO 95 05008 A (WILLEKE) 16 February 1995 see abstract see page 16, paragraph 2 - page 17, paragraph 2 see figure 8 --- -/--	1,6-10, 12

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 April 1999	06/05/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	SLEIGHTHOLME, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/GB 99/00018

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 00442 A (UNIV WASHINGTON) 3 January 1997 see page 27, line 1 - line 23 see page 44, line 24 - page 45, line 6 see figures 5,6	1,6,11
A	US 5 099 311 A (BONDE) 24 March 1992 see column 4, line 58 - line 64 see column 5, line 28 - line 45 see figures 2,3,6,7	1,2,13, 21,24,25
A	US 5 681 484 A (CHERUKURI) 28 October 1997 see column 13, line 61 - column 14, line 18; figures 11A-D	1,13,25
A	US 5 152 060 A (BICHLER) 6 October 1992 see abstract; figure 2	8,9
A	WO 96 12541 A (BULL) 2 May 1996 cited in the application see abstract; figure 1A	23

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte onal Application No
PCT/GB 99/00018

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 19511603 A	02-10-1996	WO 9630113 A	03-10-1996
		EP 0879083 A	25-11-1998
WO 9505008 A	16-02-1995	DE 4426347 A	02-02-1995
		EP 0742959 A	20-11-1996
		JP 9501268 T	04-02-1997
		US 5704992 A	06-01-1998
WO 9700442 A	03-01-1997	AU 6541596 A	15-01-1997
		CA 2222126 A	03-01-1997
		EP 0839318 A	06-05-1998
US 5099311 A	24-03-1992	NONE	
US 5681484 A	28-10-1997	US 5585069 A	17-12-1996
		AU 4152396 A	06-06-1996
		AU 4233796 A	06-06-1996
		CA 2204912 A	23-05-1996
		CA 2205066 A	23-05-1996
		EP 0791238 A	27-08-1997
		EP 0808456 A	26-11-1997
		JP 11500602 T	19-01-1999
		WO 9615450 A	23-05-1996
		WO 9615576 A	23-05-1996
		US 5643738 A	01-07-1997
		US 5593838 A	14-01-1997
		US 5846396 A	08-12-1998
		US 5755942 A	26-05-1998
		US 5863708 A	26-01-1999
		US 5858804 A	12-01-1999
US 5152060 A	06-10-1992	DE 3709278 A	29-09-1988
		AT 75980 T	15-05-1992
		WO 8806941 A	22-09-1988
		EP 0391895 A	17-10-1990
		JP 2854309 B	03-02-1999
		JP 3500861 T	28-02-1991
		US 5249359 A	05-10-1993
WO 9612541 A	02-05-1996	AT 175362 T	15-01-1999
		AU 695237 B	13-08-1998
		AU 3703095 A	15-05-1996
		AU 699883 B	17-12-1998
		AU 3703195 A	15-05-1996
		CA 2203282 A	02-05-1996
		CA 2203283 A	02-05-1996
		DE 69507157 D	18-02-1999
		EP 0787029 A	06-08-1997
		EP 0790849 A	27-08-1997
		WO 9612540 A	02-05-1996
		JP 10507406 T	21-07-1998
		JP 10507962 T	04-08-1998